22. (Twice Amended) The method of claim 20, wherein said antiviral protein conjugate or said antiviral peptide conjugate comprises (i) an amino acid sequence of SEQ ID NO: 2 or an antiviral fragment thereof comprising at least nine contiguous amino acids of SEQ ID NO: 2, and (ii) an isolated and purified viral envelope glycoprotein.

Please add the following claims:

28. (New) The method of claim 20, wherein said antiviral protein conjugate or said antiviral peptide conjugate comprises (i) an amino acid sequence of SEQ ID NO: 2 or an antiviral fragment thereof comprising at least nine contiguous amino acids of SEQ ID NO: 2, and (ii) a virus.

29. (New) The method of claim 28, wherein the virus is a retrovirus.

30. (New) The method of claim 29, wherein the retrovirus is an immunodeficiency virus.

31. (New) The method of claim 30, wherein the immunodeficiency virus is HIV-1 or HIV-2.

REMARKS

The Present Invention

The present invention is directed to a method of inhibiting binding of an enveloped virus to a cell in a host. The method comprises administering to the host an antiviral effective amount of an isolated and purified antiviral agent selected from the group consisting of an antiviral protein, an antiviral peptide, an antiviral protein conjugate, and an antiviral peptide conjugate, wherein said antiviral protein or antiviral peptide has an amino acid sequence of SEQ ID NO: 2 or an antiviral fragment thereof comprising at least nine contiguous amino acids of SEQ ID NO: 2, whereupon administration of said antiviral effective amount of said antiviral agent, binding of the enveloped virus to the cell is inhibited.

Amendments to the Claims

Claims 20 and 22 have been amended to point out more particularly and claim more distinctly the present invention. The amendments to claims 20 and 22 are supported by the specification at, for example, page 8, lines 3-8, page 11, line 30, through page 12, line 2, page 14, lines 27-31, page 19, lines 22-28, page 21, lines 15-22, page 22, lines 7-20, page 35, line

36, through page 36, line 3, and Examples 5 and 6. Claims 28-31 have been added and are supported by the instant specification at, for example, page 3, lines 30-33, page 5, lines 8-15, page 5, line 31, through page 6, line 4, page 9, lines 16-22, page 11, line 23, through page 12, line 10, page 12, lines 16-19, page 14, lines 2-7, page 18, lines 16-36, page 20, lines 26-33, page 21, lines 6-15, page 21, line 23, through page 22, line 20 *et seq*, page 26, line 33, through page 27, line 5, page 27, lines 23 *et seq*, and page 28, line 15, through page 35, line 9, and by Examples 1, 4, 5, and 6. Separate documents setting forth the precise changes to the claims as well as the text of the pending claims are submitted herewith.

The Pending Claims

Claims 20-31 are currently pending and are directed to the method of inhibiting binding of an enveloped virus to a cell in a host.

Examiner Interview

Applicant wishes to thank Examiner Parkin for the courtesy of the telephonic interview of October 18, 2002. Applicant is most appreciative of the Examiner's time in discussing the matters set forth in the Office Action and herein with Applicant's representatives Heather R. Kissling and Carol Larcher.

The Office Action

The Office has rejected claims 20-27 under 35 U.S.C. § 112, first paragraph. Claims 20 and 21 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 20-24 of Application No. 09/428,275. Reconsideration of this rejection and this provisional rejection is hereby requested.

Discussion of Rejection under 35 U.S.C. § 112, first paragraph

Claims 20-27 have been rejected under Section 112, first paragraph, for alleged lack of enablement. This rejection is traversed for the reasons set forth below.

The Office contends that the instant specification provides insufficient guidance as to which regions of the cyanovirin peptide are required for antiviral activity. The Office points out that the pending claims encompass any mutant of cyanovirin (CV-N). As amended, the inventive method involves administration of an antiviral protein or antiviral peptide having an amino acid sequence of SEQ ID NO: 2 or an antiviral fragment thereof comprising at least nine contiguous amino acids of SEQ ID NO: 2. This claim amendment has not been proposed previously. Applicant provides nucleic acid and amino acid sequences encoding

cyanovirins in SEQ ID NOS: 1-4 and Figure 2, for example. As required by the pending claims, the amino acid sequence of SEQ ID NO: 2 or the fragment thereof comprising at least nine contiguous amino acids of SEQ ID NO: 2 have antiviral activity. Methods of screening candidate proteins and peptides for antiviral activity are provided in the instant specification at, for example, page 24, line 19, through page 25, line 25, and in Examples 5 and 6. Specifically, Example 5 provides a method for determining a candidate peptide's ability to inhibit the cytopathic effects of a virus, HIV-1, upon human cells, while Example 6 provides a method to determine the ability of a candidate peptide to interrupt cell-virus binding. The methods involve routine laboratory techniques that are well within the skill of the ordinary artisan. Indeed, the Office has provided no evidence that undue experimentation would be required to identify an antiviral protein or antiviral peptide for use in the inventive method.

The Office further contends that the instant specification fails to provide sufficient guidance with respect to the binding specificity of CV-N, and it is allegedly not clear that CV-N can bind to all viruses. Solely in an effort to advance prosecution of the instant application, the pending claims have been amended to recite a method of inhibiting binding of an enveloped virus to a cell in a host. Applicant has demonstrated that cyanovirins can bind to a variety of viruses. In particular, it has been demonstrated that CV-N binds to the carbohydrate moieties of viral surface glycoproteins from which the proteinaceous component has been removed (see Declaration under 37 C.F.R. § 1.132 of August 6, 2001). The Office has provided no evidence to dispute the data presented in the Declaration or cast doubt on the ability of CV-N to bind to viruses other than those specifically described in the Declaration. The Office merely states that it is not clear that CV-N binding can be extended to all other viruses without providing any scientific evidence in support of its contention. In this regard, Applicant points out that binding of CV-N to HIV, Ebola, and *Herpes Simplex* virus has been demonstrated and that these viruses represent very distinct families of viruses, namely *Retroviridae*, *Filoviridae*, and *Herpesviridae*, respectively. The ability of CV-N to bind to such diverse viruses provides a reasonable basis for the ordinarily skilled artisan to believe that CV-N can bind to other, equally diverse, viruses.

The Office further contends that the *in vitro* assay provided in the specification is not predictive of clinical efficacy with respect to inhibiting a viral infection. The references cited by the Office which allegedly teach that *in vitro* assays are not predictive of clinical success do not pertain to the *in vitro* assay disclosed in the instant specification. The specific reference cited in the Office Action relates to structure-based drug design, which is not equivalent to the HIV screening assay provided. The Office has provided no scientific evidence that casts doubt on the assay provided in the specification as being predictive of *in vivo* results. In fact, the *in vitro* assay is predictive of *in vivo* results, as the ability of the

antiviral agent to inhibit a viral infection has been demonstrated in two different animal models involving two different viruses. The Office alleges that the data provided by way of Declarations under 37 C.F.R. § 1.132 submitted February 5, 2001, and January 30, 2002, do not accurately predict inhibition of a viral infection therapeutically or prophylactically (Office Action, Section 6). Yet, the only reference cited by the Office (Rice and Bader, 1995) is solely directed to *in vitro* assays and does not discuss any *in vivo* models, much less the macaque model or mouse model described in the Declarations under 37 C.F.R. § 1.132. Thus, the Office has not provided any evidence in support of its contention that the animal models are not predictive of clinical success.

However, solely in an effort to advance prosecution of the instant application and not in acquiescence of the rejection, the claims have been amended to recite a method of inhibiting binding of an enveloped virus to a cell in a host. Examples 5 and 6 of the instant specification, as well as the data provided to the Office by way of the Declarations submitted February 5, 2001, August 6, 2001, and January 30, 2002, clearly demonstrate the ability of CV-N to inhibit binding of an enveloped virus to a cell in a host.

For the reasons set forth above, the applicant respectively submits that the presently claimed invention is enabled by the instant application. Therefore, Applicant requests the withdrawal of the rejection under Section 112, first paragraph.

Discussion of Provisional Obviousness-Type Double Patenting Rejection

Claims 20 and 21 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 20-24 of Application No. 09/428,275. This rejection will be addressed upon indication of allowable subject matter.

Conclusion

The application is considered to be in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If any issues remain regarding patentability of the pending claims, Applicant's representative respectfully requests a telephonic interview.

Respectfully submitted,

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Date: October 30, 2002

CERTIFICATE OF MAILING

I hereby certify that this AMENDMENT AND RESPONSE TO OFFICE ACTION (along with any documents referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231.

Date: Oct. 30, 2002

Catherine M. Cioffi